Remarks/Arguments

After the instant amendment, claims 1-36 are currently pending in the application, and claims 7, 9, 10-11, 13-14, 16, 18, 19-24, 34, and 36 are amended.

Objections to the Specification

The Examiner objects to various aspects of the specification. The specification has been amended to overcome the Examiner's objections. No new matter has been added by these amendments.

Claim Objections

The Examiner has objected to claims 22 and 23 over informalities. Claims 22 and 23 have been amended to correct the typographical errors cited by the Examiner.

Claim 34 was objected to as being an improper multi-dependent claim dependent upon other multi-dependent claims. The claim dependency has been amended and the Examiner is requested to reconsider this claim in its amended form.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 36 stands rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite because of the use of Triton X-100 as a limitation rather than the chemical formula. This claim has been amended to include the chemical formula and the Trade name is being retained in parentheses for clarity.

Claim 7 stands rejected under 35 U.S.C. § 112, second paragraph for lack of antecedent basis for the word "porin" in the wherein clause. Applicant has amended claim 7 to depend from claim 6, thus amended claim 7 does not lack antecedent basis for the word "porin".

Claims 9-14, 16, and 18-24 stand rejected under 35 U.S.C. § 112, second paragraph as indefinite because the claims recite the phrase "any of claims" but only cite one claim. Claims 9-14, 16, and 18-24 have been amended to only refer to a single claim.

Claim 23 stands rejected under 35 U.S.C. § 112, second paragraph as indefinite for lack of antecedent basis for the term "integral membrane protein". Claim 23 has been amended to depend from claim 22, thus the phrase "integral membrane protein" now has antecedent basis.

Claims 8-24 and 26-33 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. In the rejection, it is stated "[i]t is unclear how one "exchanges", one detergent for a nonionic detergent, but then later "keeps" the zwitterionic detergent which one has removed in a previous step."

Applicant points out that these are independent and separate "altering" processes as described in the specification on page 18, line 29 though page 19, line 2. The altering process is defined as

> *the process of improving the tolerability of an immunogenic composition by one of the following methods: (i) diluting the zwitterionic detergent, (ii) exchanging the zwitterionic detergent with a non-pain causing nonionic detergent, or (iii) adding a non-pain causing nonionic detergent but keeping the concentration of the zwitterionic detergent constant.*

The claim language in question is definite when it is read as a Markush claim where category (ii) refers to a process of exchanging of one lipid for another and category (iii) is an alternative that refers to a separate process of adding a non-pain causing detergent to but keeping the concentration of the zwitterionic detergent (pain causing) constant. The two processes are not intended to be carried out simultaneously on the same sample as the Examiner surmised.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-33, 35 and 36 stand rejected 35 U.S.C. § 112, first paragraph as allegedly lacking enablement for "*any/all other zwitterionic agents or any/all other ionic detergents.*" It is further stated "*[t]he only working examples utilize Zwittergent 3-14 and Triton X-100.*"

Applicants respectfully traverse this rejection. The specification provides extensive guidance and working examples on how to select and test any detergent sought to be used in practicing the invention. For example, the rat footpad model for determining whether any immunogenic formulation is pain causing or tolerable is described in Example 1, page 31, line 16 through Example 3, page 42, line 11. These three examples describe the effect of other variables such as detergent concentration at or above the critical micelle concentration, volume of injected formulation and immunogenic protein. Examples 4 though 8 provide additional guidance on the effects of detergent and protein concentration and three specific methods of improving the tolerability of various painful formulations.

The rejection further states *"[t]he amount of direction/guidance/working examples present in the instant application is insufficient support for the broad scope of the instant claims. The only working examples utilize Zwittergent 3-14 and Triton X-100"*. Applicants respectfully submit that this rejection is inapplicable because Example 9 on page 53, line 15 though page 55, line 5 and tables 15-17 entitled "*Tolerability of Various Detergents*" provide many more than two examples of detergents that either are pain-causing or non-pain causing. This example details the pain causing characteristics of 14 different Zwitterionic and non-ionic detergents. Therefore, applicants request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-33, 35 and 36 stand rejected 35 U.S.C. § 112, first paragraph as allegedly lacking enablement "*because the specification, while being enabling for the specific agents utilized in the examples at the specific doses recited, does not reasonably provide enablement for any/all other doses of zwitterionic agents or any/all nonionic detergents.*"

Applicants respectfully request that this rejection be reconsidered and withdrawn, because as the specification makes clear, the invention is based on many variables such as the nature and concentration of the detergents involved and their critical micelle concentrations. The critical micelle concentration of a detergent is in turn dependent, among other things, on the temperature and the concentration of other lipids and detergents in the solution and the presence or absence of mixed micelles. Dose is not one of the variables or limitations in any of the claims. The critical parameter is whether the formulation causes too much pain or whether it is tolerable. The specification provides the tools for one of skill in the art to determine whether they are practicing the invention or not.

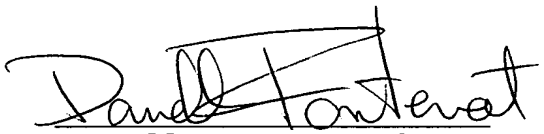
The specification provides working examples on all of the limitations of the claims and how to create compositions of perform the methods of the claims. For example, the rat footpad model for determining whether any immunogenic formulation is pain causing or non-painful is described in Example 1, page 31, line 16 through Example 3, page 42, line 11 and describes how to measure pain and the effect of other variables such as detergent concentration at or above the critical micelle concentration, volume of injected formulation and immunogenic protein on the pain. Examples 4 though 8 provide guidance on the effects of various detergents and protein concentrations and three specific methods of improving tolerability of various painful formulations. Example 9 on page 53, line 15 though page 55, line 5 and tables 15-17 entitled "*Tolerability of Various Detergents*" provide additional examples of detergents that either are pain-causing or non-pain causing.

In addition, the detailed description provides additional guidance on zwitterionic detergents on page 13, line 21 through page 14, line 8; non-ionic detergents are provided on page 15, line 5 through page 16, line 3. Altering a painful composition and concentrations of zwitterionic and non-ionic detergents are detailed on page 18, line 21 through page 21, line 3.

Conclusion

It is therefore requested that the Examiner consider the patentability of all of the above claims. If the Examiner believes a telephone conference would expedite prosecution of this application, the Examiner is requested to contact the undersigned attorney at 845-602-3144.

Respectfully submitted,



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